REMARKS

Claims 7, 13 and 15-21 are pending. Claims 8, 9, 12, 14 and 23 have been cancelled and claims 7 and 13 have been amended. In particular, claims 7 and 13 have been amended to require that the mixture of fragmented DNAs is prepared by hydrodynamic point-sink shearing method as supported by claims 9 and 14, now cancelled. Further, claims 7 and 13 have been amended to require that the mixture of fragmented DNAs is a mixture of DNAs having an average size of from 0.5 kbp to 2.5 kbp as supported by cancelled claims 12 and 23 as well as the present specification at page 15, lines 1-8. Lastly, claim 13, step (c) has been amended in order to clarify the nature of this step. Accordingly, no new matter has been added.

In view of the following remarks Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Issues under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 13-21 and 23 under 35 U.S.C. §112, second paragraph for the reasons recited at page 3 of the outstanding Office Action. Applicants respectfully traverse.

First, the Examiner has asserted that the phrase including the term "abundance ratio" is indefinite since this term is allegedly not defined in the claims or specification. Applicants respectfully disagree with the Examiner. For instance, the present specification at page 11, lines 15-24 specifically describes the abundance ratio as well as a method for determining whether or not the genomic DNA of the present invention maintains the copy numbers for a set of genes or sequences in a genomic DNA. Additionally, Applicants further draw the Examiner's attention to

the fact that the term "abundance ratio" is a term commonly used by those of skill in the art. As evidence of this, Applicants attach hereto the reference, Putkey et al., *The Journal of Biological Chemistry*, Vol. 258, No. 19, pp. 11864-11870 (1983). In this reference, the term "abundance ratio" is utilized, for instance, see line 11 from the bottom of the Abstract, without any specific definition. Those of skill in the art can readily determine the "abundance" of genes or sequences by known methods for quantitative determination or analysis of nucleic acids, and readily compare the thus determined "abundance" of genes or sequences. Accordingly, Applicants respectfully submit that the "abundance ratio" is sufficiently clear to those of skill in the art.

Second, the Examiner has rejected claim 13, as well as claims 14-21 and 23 which depend thereon, asserting that the nucleic amplification step is unclear as to whether or not the DNA fragments are templates and primers or only templates. Applicants respectfully traverse and submit that claim 13 has been amended to clarify that the DNA fragments obtained in step (b) are subjected to nucleic acid amplification using amplification primers. Similar language has been used and accepted in claim 7 of the present application.

In view of the above, Applicants respectfully submit that the present claims are fully definite. Accordingly, the Examiner is respectfully requested to withdraw these rejections.

Issues under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 7-9, 12, 13, 15-21 and 23 under 35 U.S.C. §112, first paragraph for the reasons recited at pages 4-8 of the outstanding Office Action. Applicants respectfully traverse.

The Examiner maintains that the specification enables only the hydrodynamic point-sink shearing method as a fragmentation method but not other methods. Although Applicants continue to disagree with the Examiner on this point, to expedite prosecution, Applicants have amended independent claims 7 and 13 in order to indicate that the fragmentation method is a hydrodynamic point-sink shearing method. Accordingly, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues under 35 U.S.C. §103(a)

The Examiner has rejected claims 7-9 and 13-16 under 35 U.S.C. § 103(a) as being obvious over Oefner et al., *Nucleic Acids Research*, 1996, Vol. 24, No. 20, pages 3879-3886 (hereinafter referred to as Oefner) in view of Lucito et al., *PNAS*, 1998, Vol. 95, pages 4487-4492 (hereinafter referred to as Lucito). Applicants respectfully traverse this rejection.

The Present Invention as Defined by Claims 7 and 13

Claim 7 of the present invention relates to a method for producing a genomic DNA library, comprising the steps of (1) preparing a mixture of fragmented DNAs having distribution ratio of 1 to 5 as defined by the size ratio (distribution ratio) of the maximum size of fragmented DNA to the minimum size of fragmented DNA and having a size convergence rate of 80% or more, wherein said mixture of fragmented DNAs is prepared by hydrodynamic point-sink shearing method, and wherein said mixture of fragmented DNAs is a mixture of DNAs having an average size of from 0.5 kbp to 2.5 kbp; and (2) subjecting the mixture of fragmented DNAs obtained in step (1) to nucleic acid amplification using amplification primers, thereby producing

DNAs corresponding to said mixture of fragmented DNAs, to give a genomic DNA library maintaining 85% or more of copy numbers of a set of genes or sequences on a genomic DNA and an abundance ratio of said set of genes or sequences on the genomic DNA.

Moreover, an additional method is recited in independent claim 13, which relates to a method for producing a genomic DNA library, comprising the steps of: (a) preparing a mixture of fragmented DNAs having distribution ratio of 1 to 5 as defined by the size ratio (distribution ratio) of the maximum size of fragmented DNA to the minimum size of fragmented DNA and having a size convergence rate of 80% or more, wherein said mixture of fragmented DNAs is prepared by hydrodynamic point-sink shearing method, and wherein said mixture of fragmented DNAs is a mixture of DNAs having an average size of from 0.5 kbp to 2.5 kbp; (b) ligating adapter DNA to the fragmented DNAs obtained in step (a), thereby giving DNA fragments; and (c) subjecting the DNA fragments obtained in step (b) to nucleic acid amplification using amplification primers, thereby producing DNAs corresponding to said mixture of fragmented DNAs, to give a genomic DNA library maintaining 85% or more of copy numbers of a set of genes or sequences on a genomic DNA and an abundance ratio of said set of genes or sequences on the genomic DNA.

Distinctions Between the Present Invention and the Cited Art

All previously submitted arguments are herein incorporated by reference. Applicants continue to maintain that there is insufficient motivation to combine the references of Oefner and Lucito as suggested by the Examiner. That is, Oefner fails to suggest or disclose the specification amplification primers required by independent claims 7 and 13 of the present

invention. Lucito is unable to cure this deficiency. Based upon this deficiency alone, there exists no *prima facie* case of obviousness.

Moreover, Applicants draw the Examiner's attention to the fact that according to the present claims, the mixture of fragment and DNAs is a mixture of DNAs having an average size of from 0.5 kbp to 2.5 kbp. The primary reference of Oefner discloses a method for subcloning the fragmented genomic DNA to a plasmid vector by fragmenting a genomic DNA using a hydrodynamic point-sink shearing method. At Fig. 2 and Fig. 3 in Oefner, fragmented DNAs of about 300-12 kbp are disclosed. Oefner, however, fails to suggest or disclose which length of fragments would be suitable to maintain copy numbers of a set of genes or sequences on a genomic DNA and an abundance ratio of the set of genes or sequences on the genomic DNA in case that nucleic acid fragments are amplified by nucleic acid amplification using amplification primers.

In Lucito, it is disclosed that the genomic DNA is cleaved by restriction enzyme and the adaptors are ligated to the obtained DNA fragments, followed by carrying out PCR to provide a library. At Fig. 2 in Lucito, cleaved DNA fragments having different lengths by digestion with a 6 base pair cutter and digestion with a 4 base pair cutter are disclosed. Lucito, however, also fails to disclose or suggest which length of fragments would be suitable to maintain copy numbers of a set of genes or sequences on a genomic DNA and an abundance ratio of the set of genes or sequences on the genomic DNA.

In contrast, according to the present invention, the claims require that fragmented DNAs having an average size of from 0.5 kbp to 2.5 kbp are obtained by the present invention. By fragmenting DNAs to those having this average size, with regard to amplified DNA fragments,

copy numbers of a set of genes or sequences on a genomic DNA and an abundance ratio of the set of genes or sequences on the genomic DNA can be maintained. Thus, according to the present invention, it becomes possible to produce a genomic DNA library where the composition of fragmented genomic DNA is unchanged even after repeated amplifications. However, Oefner and Lucito fail to suggest or disclose the particular average size of from 0.5 kbp to 2.5 kbp according to the presently claimed methods. Thus, these references fail to provide the basis for a *prima facie* case of obviousness. Moreover, due to the lack of recognition of the presently claimed limitations, the references of Oefner and Lucito further fail to recognize a method for obtaining the presently claimed method including copy numbers and abundance ratios. Accordingly, Applicants submit that the rejection based upon Oefner and Lucito is improper and should be withdrawn.

Further, the Examiner has rejected claims 17-21 and 23 under 35 U.S.C. §103(a) as being obvious over Oefner in view of Lucito and Sorge et al. (USP 5,556,772). Applicants respectfully traverse this rejection.

As pointed above, the references of Oefner and Lucito fail to recognize the presently claimed subject matter. The secondary reference of Sorge '772 is unable to cure these deficiencies. Accordingly, this rejection is improper for the same reasons as the above rejection. Reconsideration and withdrawal of this rejection are therefore requested.

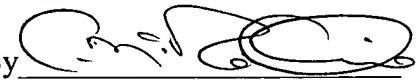
In view of the above, Applicants respectfully submit that the present claims define allowable subject matter. Accordingly, the Examiner is respectfully requested to withdrawal all rejections and allow the currently pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie (Reg. No. 42,874) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Dated: February 14, 2006

Respectfully submitted,

By 

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Attachment: "Chicken Calmodulin Genes", Putkey et al.